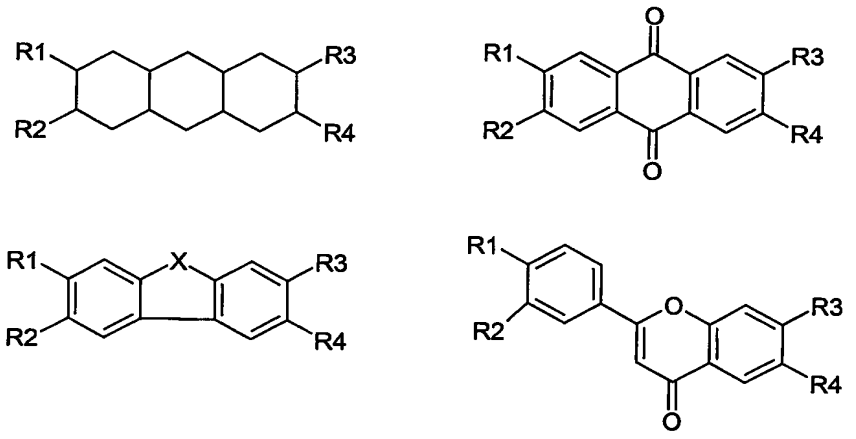
CLAIMS

What is claimed is:

1. A novel pharmacophore model as defined by the parameters of Table 4 and Table 5.

2. The novel pharmacophore model of claim 1, wherein scaffold molecules derived therefrom can be used as a basis for compounds directed to inotropic Na, K-ATPase inhibition.

3. The novel pharmacophore model of claim 1, wherein the model produces an Na, K-ATPase inhibitor compound of the formula:



wherein R1, R2, R3 and R4 can be any organic functional group containing a hydrogen bond donor or a hydrogen bond acceptor and X is any element or group that allows the compound to retain inotropic activity.

4. The novel pharmacophore model of claim 3, wherein X is N, O, S, or C.

5. A method of using a pharmacophore model to create an Na, K-ATPase inhibitory compound comprising the steps of:

(a) creating alignment between SERCA and Na, K-ATPase, wherein SERCA is a template;

(b) transferring coordinates from the template to a model for structurally conserved regions;

(c) generating variable regions;

(d) refining the model through energy minimization steps; and

(e) performing docking analysis of prospective drug candidates.

6. The method of claim 5, further comprising the steps of:

(f) delineating the essential pharmacophoric elements for high binding affinity;

(g) searching databases of known compounds using the restraints as implicated by the pharmacophore with allowable tolerances; and

(h) utilizing de novo rational drug design and computer aided molecular modeling to design novel compounds using the restraints as implicated by the pharmacophore with allowable tolerances.

7. The method of claim 6, wherein the allowable tolerances in steps (g) and (h) is ±10%.

8. The method of claim 5, wherein step (a) is comprised of dynamic programming and threading.

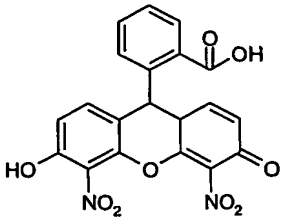
9. The method of claim 5, wherein SERCA is SERCA1a.

10. The method of claim 5, wherein the steps are carried out using a computer-readable medium having computer-executable instructions.

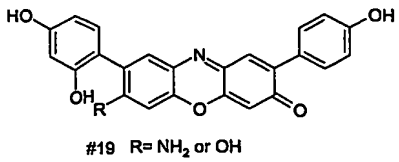
11. The method of claim 10, wherein the steps are carried out using molecular modeling software.

12. A method of treating an individual with a heart disease comprising administering a therapeutically effective amount of an novel inotropic compound created using a novel pharmacophore model as defined by Table 4 and Table 5.

13. The method of claim 12, wherein the novel pharmacophore model produces novel inotropic drugs of the formula of:

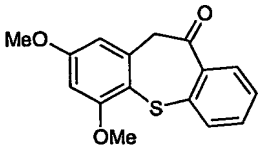


4',5' Dinitroflorescein



#19 R= NH_2 or OH

or



14. The method of claim 13, wherein the novel drugs have a wider therapeutic index than either ouabain or digoxin.

15. The method of claim 12, wherein the heart disease treated is congestive heart failure and supraventricular arrhythmia.

16. The method of claim 12, wherein the novel inotropic compound is administered in a pharmaceutically acceptable carrier.

17. The method of claim 12, wherein the novel inotropic compound is administered parenterally or orally.

18. The method of claim 12, wherein residues Q111, D121, E908 and M973 are unaltered.